

IMMUNE TO A TWENTIETH-CENTURY PLAGUE

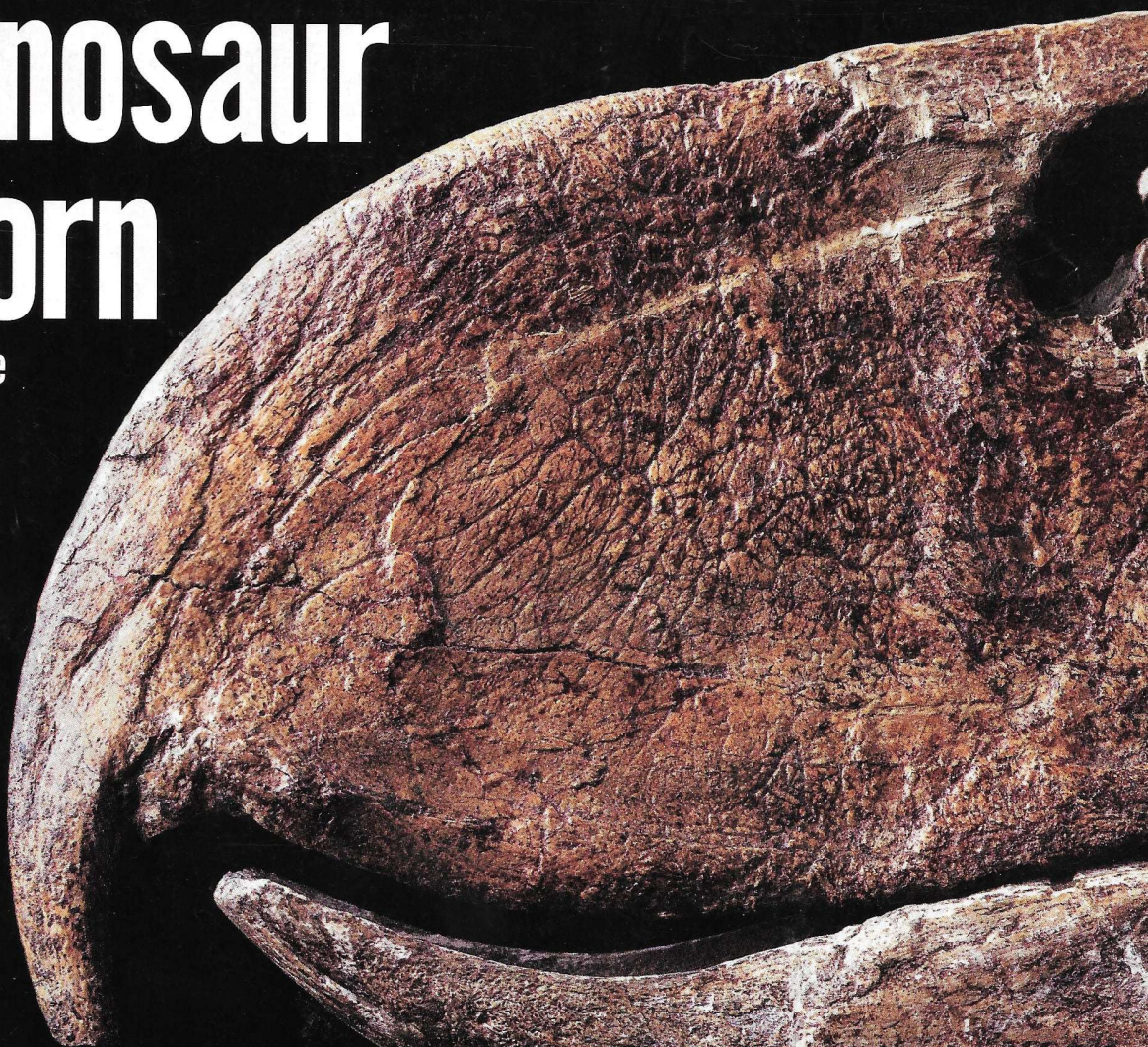
Discover

THE WORLD OF SCIENCE

JUNE 1997

A Dinosaur Reborn

Once upon a time
in America, 40
million years
after the dinos
had gone, life
really did find
a way to bring
them back —
almost.



U.S.A. \$3.95 / Can. \$4.50



GET WELL SOON

MENU
☐ MILK
☐ YOGURT
☐ RICE PUDDING
☐ MASHED POTATOES
☐ CREAM

IMMUNE TO A PLAGUE

A few lucky
individuals won't

BY PETER RADETSKY

ever contract AIDS:
they're genetically
immune. And the
more we learn about
how their genes
protect them, the
closer we come to
protecting all of us.

THE STORY BEGINS WITH A MOUSE. WITH A bunch of them, that is; a bustling colony of smallish brown field mice scurrying through the grain bins of a squab farm outside Los Angeles in 1979. They were not quite ordinary mice. They happened to carry a gene that protected them against a devastating leukemia virus that was annihilating the rest of the rodents on the farm. This gene, a "restriction" gene, barred infection by blocking the doorway—the receptor—through which the virus gained entry to the cells it attacked. Denied access, the lethal virus was left futilely hammering at the gate, harmless and vulnerable, to be destroyed in short order by the body's defenses. In

PAINTINGS BY

FRANK MOORE

other words, these mice were genetically immune to the disease.

This finding set Stephen O'Brien, a National Cancer Institute (NCI) geneticist who had helped analyze the gene, to thinking: If mice could carry a gene that protected them against a deadly viral invasion, why couldn't we? In 1979 there was no way to find out, since no comparable human outbreak had come along. But soon enough history offered up an exemplary epidemic: the scourge of AIDS. By 1984 it was known that the disease's cause was a fiendishly elusive virus called HIV. O'Brien responded immediately.

"I rounded up half a dozen AIDS researchers and asked them what they thought of the idea of looking for a human restriction gene. They said, 'Sounds great, but we don't know anything about human genetics.' I rounded up human geneticists and said, 'What do you think?' They said, 'This is a wonderful idea, but we're scared to work with HIV.' So I said, 'Okay, I'm going to try it.'"

O'Brien asked physicians across the country to send blood from their high-risk and infected patients to his lab in Frederick, Maryland. "They were happy to help. They just sent, and sent, and sent the stuff to us. For ten years people have been sending us blood samples. We now have in the can samples from something like 10,000 patients." For ten years O'Brien and his team have been sifting through this treasure trove of blood for a gene that protects against infection with HIV.

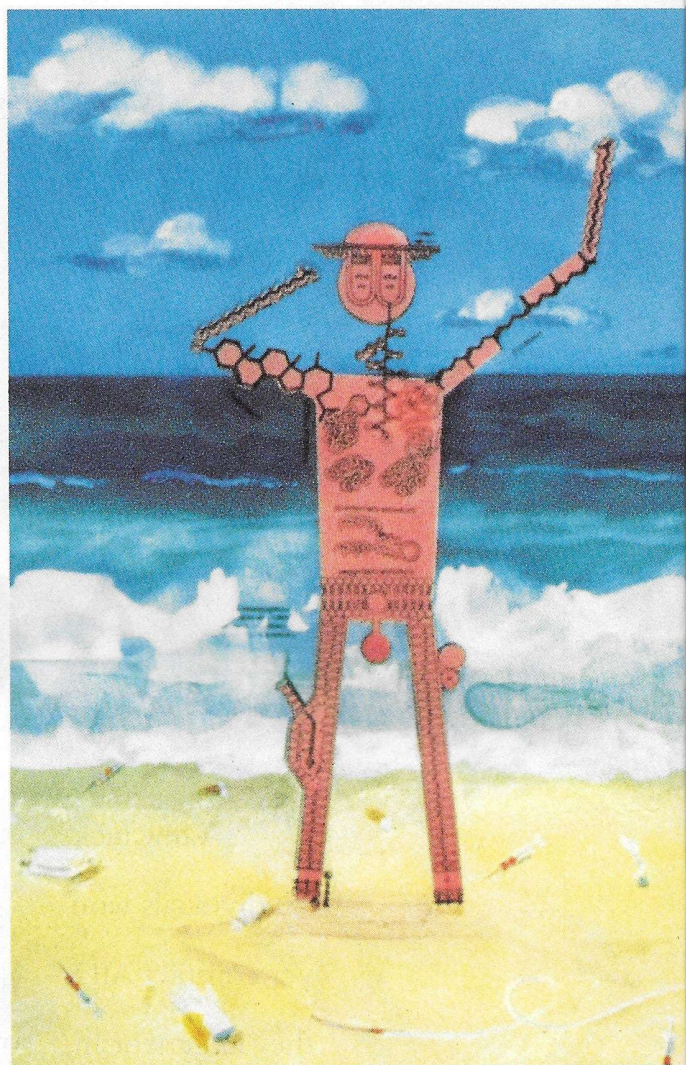
Last August he found it, with more than a little help from his friends. In the space of a year an astonishing burst of revelations by numerous scientists has transformed AIDS research, confirming the reality of genetic immunity to this terrifying disease and offering a realistic possibility of its prevention and cure. Finding the gene, however, involved more twists and turns, more coincidence and serendipity, than O'Brien could ever have anticipated. In fact, finding the gene was mostly the result of not even looking for it.

Back in 1986, when O'Brien was starting to build up his store of HIV blood samples, across the country in San Francisco, University of California virologist Jay Levy was describing some puzzling events involving HIV infection. Levy was not a geneticist; nevertheless, his findings were to provide the first lead in the hunt for the gene.

"There was a man who routinely came in to be checked for infection," Levy recalls. "We followed him for about five months, and suddenly we could no longer find virus in his blood. We didn't know what was going on. Finally we decided that maybe he's still got the virus but we were missing it because there were cells preventing it from coming out. The logical cell was the CD8 lymphocyte."

HIV infects white blood cells, or lymphocytes, called CD4 (after the name of a prominent protein on their surface). The main job of CD4 lymphocytes is to help other immune cells function. By penetrating these CD4 cells and forcing them to churn out new viruses that infect and destroy yet more cells, HIV brings the body's defense response to a grinding halt. The upshot is AIDS. Part of that defense response involves cells called CD8 lymphocytes—the killer cells and suppressor cells of the immune system. When a virus, such as HIV, infects a CD4 cell, the cell displays telltale markers on its surface. CD8 cells can recognize these cues and punctually destroy the diseased cell, or at least suppress its function. No wonder Levy suspected that CD8s might be at the heart of his patient's unexpected turnaround.

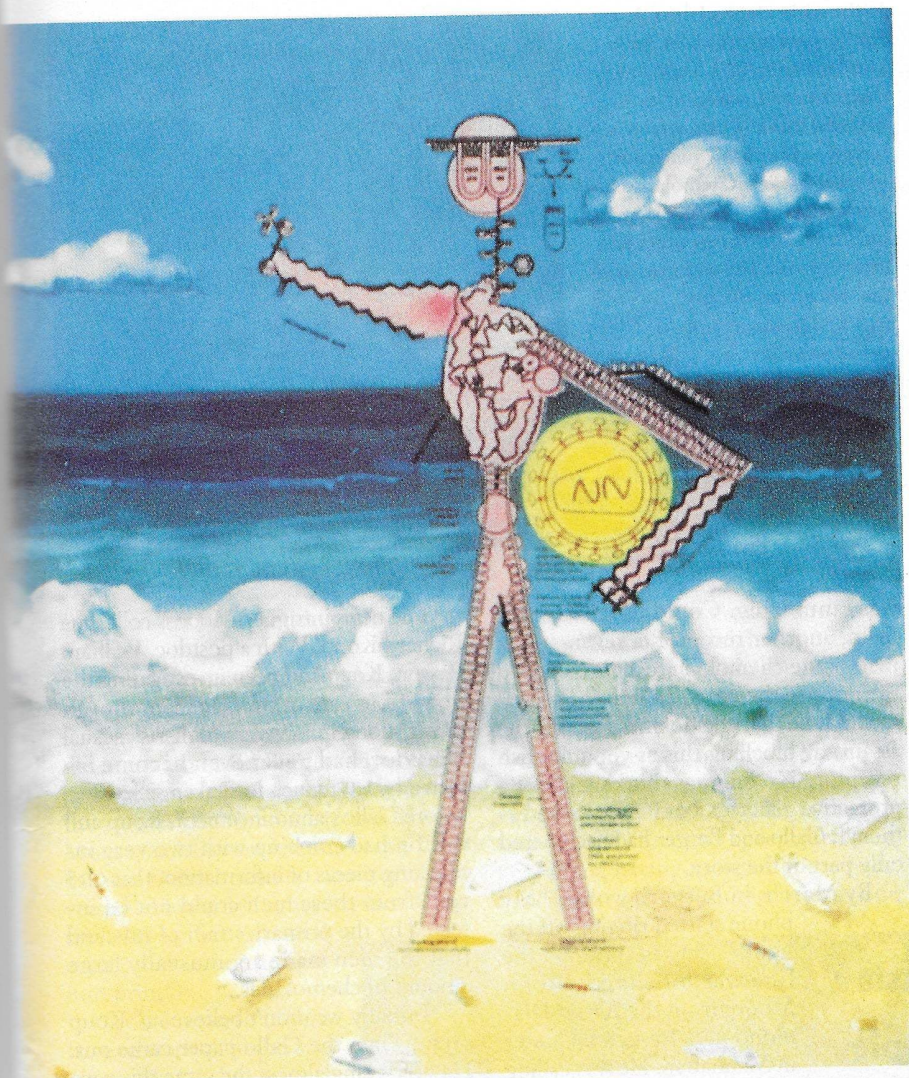
Levy investigated. "We did experiments in which we removed CD8 cells from samples of the subject's blood. It was really dramatic: virus appeared. Then we put the CD8 cells back in the blood, and the virus went away. And by this time we were seeing this same phenomenon in other people. Pull CD8s out, virus comes out—put CD8s back, virus goes away." But the CD8 cells weren't actually eliminating the CD4 cells—that is, with the CD8 cells present, the CD4 cells in the



Beach Ball

sample weren't dying. Perhaps, he thought, the CD8 cells were producing some substance that suppressed the virus, preventing it from replicating. To test that hunch, he and his colleagues put CD8 cells in a lab dish, covered them with a fine-mesh screen, then spread CD4 cells over the top. The screen kept the cells apart but allowed fluid secreted by the CD8 cells to diffuse upward to the CD4s. Sure enough, the virus disappeared.

For Levy, then, the key to stopping AIDS involved understanding CD8's role in the tortuous progression of disease. Most people infected with HIV remain healthy for years, until finally coming down with AIDS symptoms, growing weaker, and eventually dying. Levy felt that CD8 cells were the key. "The way we tied events together is this: A person gets infected with HIV, and at first the CD8s control the virus. Then for some reason the CD8s lose control, the virus comes



out, kills off CD4 cells, and the person goes on to disease."

Not many others agreed. "People didn't believe us," Levy says. "I can't explain why. Maybe because this represented a new idea in immunology. Why would you suppress and not kill?" While his colleagues looked on with a kind of bemused tolerance, Levy began a decade's search for the active substance in the CD8 reaction (he called it CAF, for CD8 antiviral factor). He had no luck. It turned out that CD8 cells, like other lymphocytes, were hard to keep alive in the lab, and they manufactured the elusive factor only once in a while, making it hard for Levy to amass enough for study. He was reduced to describing what his factor was not.

"I kept saying, 'It isn't this, this, this, or this.' But everyone kept saying, 'Why don't you tell us what it is?'" says Levy, sighing. "This has been the longest project for me."



IT MAY BE THAT ROBERT Gallo has found Levy's factor for him. In early 1995, almost ten years after Levy first described his baffling cases, Gallo—the rambunctious former NCI and current University of Maryland researcher who codiscovered HIV—and collaborator

Paolo Lusso set out to determine once and for all whether there was anything to this CAF business. They, like Levy, were not looking for an HIV-resistance gene, but what they turned up offered the second lead to its existence. "I brought up in a staff meeting that sooner or later we were going to have to look at this crazy story," Gallo says. "Levy had been talking about it for a decade. You get suspicious in this modern age when somebody talks for a decade."

Gallo's huge NCI laboratory was ideally set up for the search. From long experience, his team had cultivated a large number of CD4 cells that they could readily infect with HIV, and they had figured out how to keep CD8 cells alive. In December 1995, Gallo and Lusso announced that they had found substances secreted by CD8 lymphocytes that did indeed suppress the replication of HIV. Specifically, they stopped viruses in the blood of individuals who had just been infected—that is, they prevented HIV from establishing a beachhead in the body. There were three of these suppressive substances. They were all members of an obscure family of hormonelike molecules called chemokines, small proteins known to help cause inflammation, presumably by latching onto chemokine receptors on immune system cells and dragging them to the site of injury. Most researchers knew next to nothing about them.

"I can honestly say that I had heard of them, but barely," says Gallo. He laughs. "A chemokine expert told me that when our paper came out his mother called him. She had heard on NPR about these 'cheezokines' that Dr. Gallo had found. 'It's very important,' she said. 'You should work on it.'"

AIDS researchers agreed. They rushed to investigate the little-known proteins, in the hopes that they might be used to stop the disease.

Thus the stage was set for lead number three. In a laboratory at the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, biochemist Edward Berger was coming to the end of his own long quest: to understand how HIV enters cells. It had been suspected for over a decade that each time HIV entered a cell, this wily virus co-opted not one but two receptors on the cell surface. One receptor was CD4, the very surface protein that lent the CD4 cell its name. The other was a mystery. For years scientists, Berger among them, had been trying to uncover its identity. By December 1995, when Gallo announced his chemokine discovery, Berger was sure his team had hit pay dirt.

He had found a complicated protein, a Loch Ness monster of a protein, that snaked above and below the surface of CD4 cells seven times—thus its designation as a "seven transmembrane" protein. By somehow docking with both it and the CD4 protein, HIV could fuse with cells

and infect them. If cells lacked this protein, the virus remained outside. It must be the long-sought second receptor, thought Berger. Because it allowed virus to fuse with cells, he named it fusin.

The virus involved was different from the strain stopped by chemokines, however. Chemokines suppressed viruses encountering the body for the first time. But HIV quickly mutates in the body after infection. Fusin allowed these already flourishing viruses to spread further throughout the body during the late, symptomatic stages of disease. So although fusin was not the end of the story—HIV must have been using some other receptor to enter cells during the early stage of infection, before it had a chance to mutate—it was an important step.

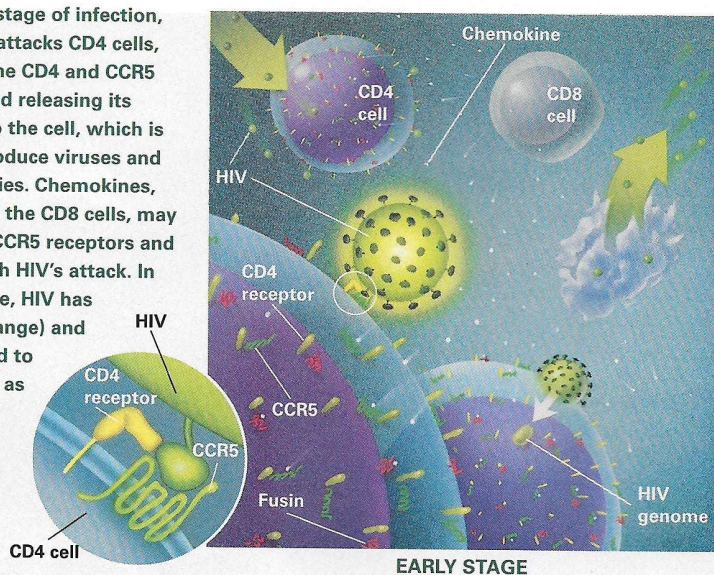
What was this odd molecule? Surely it had a function other than acting as a receptor for late-stage HIV. When Berger and his team sequenced fusin's DNA, they found that their protein was a relatively anonymous member of a huge family of similar molecules. "This family of proteins acts as receptors for extraordinarily diverse chemical processes," says Berger. "Receptors for neurotransmitters, receptors for olfaction, taste, sight. There are hundreds if not thousands of individual genes that are members of this family."

One in a hundred Caucasian Americans carries two copies of the defective chemokine receptor gene—and these people are immune to AIDS.

He pauses. "And some of them are receptors for chemokines."

Chemokines—when Berger presented his results at a meeting in February 1996, more than a few AIDS researchers began making unexpected connections. Here were Gallo and Lusso finding that certain chemokines stop viruses from infecting cells in the first place. Here was Berger announcing that fusin, a protein from a family that includes chemokine receptors, facilitated the spread of viruses that had already invaded the body. Chemokines, fusin, HIV—the connection

In the early stage of infection, HIV (green) attacks CD4 cells, binding to the CD4 and CCR5 receptors and releasing its genome into the cell, which is forced to produce viruses and eventually dies. Chemokines, produced by the CD8 cells, may bind to the CCR5 receptors and interfere with HIV's attack. In the late stage, HIV has mutated (orange) and can now bind to fusin as well as CCR5. Cells infected this way die quickly, in droves.



was tantalizing. Could it be that, like fusin, another receptor, a seven-transmembrane chemokine receptor, opened the door to the virus's initial onslaught? Could it be that chemokines stopped the assault by blocking this as yet unknown receptor? No one was thinking about a protective gene yet, but it sure looked as though Gallo and Berger had deciphered only part of the story.

By March, in Berger's words, "My phone started ringing off the hook." Among those on the line was biochemist John Moore from the Aaron Diamond AIDS Research Center in Manhattan. He was calling to congratulate Berger on his groundbreaking discovery—and to fish for information. "Ed is *Tyrannosaurus rex*," says Moore. "He killed the beast. But we weren't going to let him eat the whole thing. We were going to be raptors clawing at the carcass." Moore

and his colleagues were looking hard for a chemokine receptor.

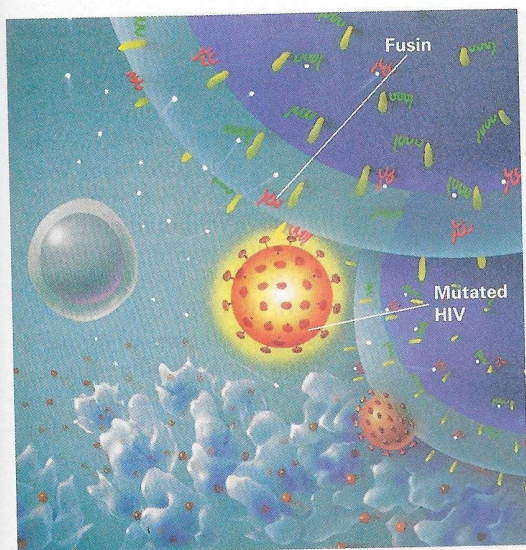
"We had read a bit about chemokines, but we knew nothing about seven-transmembrane receptors," Moore says. "In the middle of March, I went to a meeting in New Orleans and brought a huge file of reprints with me. It was my crash course, Chemokine Receptor 101. In one of the papers there was a footnote saying that a seven-transmembrane receptor called CCR5 bound one of Gallo's HIV-suppressing chemokines. That was a critical footnote."

The news intrigued Moore's colleague Richard Koup. With a postdoc, William Paxton, Koup had been investigating the mysterious case of two gay men who, although long involved in high-risk sexual behavior, had never even become infected by HIV, much less taken sick. Even before Gallo's announcement, Koup and Paxton had come up with two very interesting pieces of information: that CD4 cells from these men could not be infected by the primary strain of HIV, and that the men made an unusually large amount of chemokines.

"Initially we didn't believe it," Koup says. "Then the Gallo paper came out. He was seeing almost the same thing we were seeing. Lights went off in our heads."

Lights also went off in the head of Diamond researcher Nathaniel Landau. "When I thought about it, it made sense that chemokines might be the key," he says. "By binding to a chemokine receptor, they might block HIV. It just started smelling like the right thing."

What ensued was what Landau calls "one of the most fascinating chapters in the development of science." In the space of two weeks in late June, researchers from five different labs independently announced that they had found the co-receptor on CD4 cells that enabled HIV to establish its initial foothold in the body. It was indeed a chemokine receptor. And not just any chemokine receptor, but the very one Moore had come upon in the footnote, the seven-transmembrane protein CCR5—the docking site for the chemokines that Gallo had found



LATE STAGE

instrumental in preventing infection in the lab.

The discovery came from the University of Pennsylvania, from the Dana-Farber Cancer Institute in Boston, from the NIAID lab of Ed Berger (who hit the jackpot again), and from two teams at the Aaron Diamond Institute. Koup, Moore, and Paxton led one team, Landau and Dan Littman of New York University's Howard Hughes Medical Center led the other. All raced each other to be the first into print.

"You know that you have to work all night, and all weekend, because if you're not one of the first people in print, you're nowhere," says Koup. "I don't think there's ever been a scientific discovery where the data were generated as quickly, and were out in print as quickly, as this. And by so many people. It was just amazing."

Landau agrees. "Dan and I were writing our paper as fast as possible, sending it back and forth by E-mail. I was sleeping in my office—I have a sleeping bag under my desk. We had arranged a courier to transport the paper overnight to the journal *Nature* in London. He was supposed to come here at three in the after-

noon, and we were still working on the paper at two. Then at 2:30 our E-mail system broke down. And the courier showed up. I went crazy, screaming at the computer guy to fix the system. Finally it fixed itself. The manuscript wasn't in such good shape, but we sent it anyway." He laughs. "It was pretty funny when we got the reviews back. One of the reviewers said, 'Out of 15 authors, couldn't any of them have proofread this manuscript?'"

This white-hot explosion of discoveries revolutionized AIDS research. For one thing, the finding that HIV used CCR5 as a coreceptor reinforced the researchers' suspicions about how the chemokines might suppress infection. By docking onto the receptor, they might block HIV from doing the same thing.

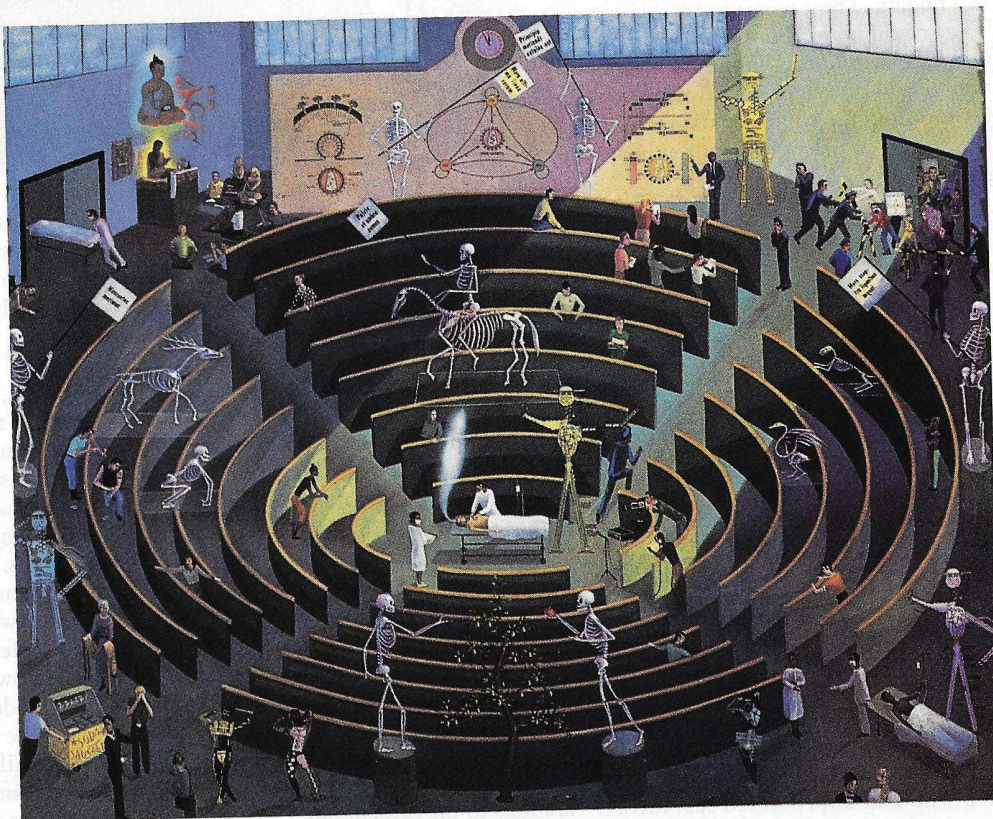
For another, it explained a great deal about the progression to disease. The virus initially infects CD4 cells via the CD4 protein and the CCR5 receptor. Then, years later, having mutated in the body, it learns how to use another receptor on

CD4 cells as well—fusin. And somehow this new route of infection signals a sea change. Once the virus learns to use fusin, cells begin to die off at an alarming rate. People get sick—the symptoms of AIDS appear. And because fusin appears on a wide variety of cells, not just CD4 lymphocytes, these symptoms become many and varied.

"For example, we know that fusin is expressed in very high levels throughout the central nervous system and the brain," says Dan Littman. "Late in the disease many people get neurological symptoms—AIDS dementia. When the virus adapts to fusin, it might trigger some harmful signal that leads to the destruction of the nervous system, though this is still very speculative."

And now scientists began to glean details of how the virus initially enters cells. Says Moore, "The CD4 receptor sticks up from the cell, while CCR5 keeps close to the surface. The virus binds to CD4 like a blimp docking at the top of the Empire State Building. But you need to get it way down to the subway station on 34th Street—that's CCR5—so the passengers can get off. Otherwise you just have a blimp stuck to the top of the building." The virus and the surface of the cell change shape, allowing

Arena



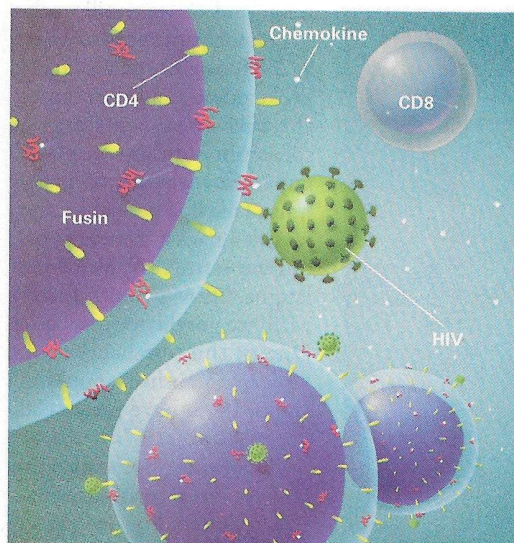
the blimp to drop down to the subway station.

Still, however, none of these researchers was thinking about protective genes. Finally that was about to change. "We said, 'Now let's figure out these exposed-uninfected individuals,'" recalls Koup. "Why can't they be infected by HIV? Maybe it was because their coreceptors don't work."

He was right. In August, when he and Landau discovered why, they suddenly found themselves face-to-face with a gene. It turned out that the gene for the patients' CCR5 receptor was defective. It sported a hole smack-dab in the middle of its DNA. The result was a CCR5 protein so badly deformed that the cell destroyed it instead of displaying it on its surface. No wonder the patients were resistant to infection—without the CCR5 receptor, HIV couldn't get its genetic material down from the top of the Empire State Building. As with O'Brien's mice, the defective gene protected them.

Genetic immunity to HIV was a bombshell of a discovery. No one had foreseen it. No one had intended it. It was the serendipitous result of a haphazard succession of seemingly unrelated revelations. But for all the researchers' excitement, it was still an extremely limited finding. These were just two people. They could be freaks of nature. To determine whether this immunity was authentic and prevalent, many more people would have to be scrutinized. As Koup says, "It was time to look at bigger populations."

RENTER STEVE O'Brien. For ten years he had been combing through his vast reserves of blood samples, looking with scant success for the tiniest hint of a resistant gene. The discovery of the CCR5 receptor galvanized him. This wasn't just a hint—it was shout, a bellow, a clarion call. His lab was poised for just such an eventuality. And O'Brien pounced. By August, when Koup and Landau announced their news, O'Brien had already submitted for publication a study of blood samples from some 1,955 high-risk individuals. They included gay men who had unprotected sex, intra-



Since early-stage HIV needs CCR5 to infect CD4 cells, people who lack that receptor are protected from infection.

venous drug users who shared needles, hemophiliacs who received tainted blood products. This investigation would pin down the truth of genetic immunity to HIV one way or another.

The results were astounding. There is indeed a defective chemokine receptor gene, and it does indeed confer resistance to the virus. Moreover, this genetic immunity is surprisingly widespread. We carry in our cells two copies of almost every gene, one inherited from our mother, one from our father. O'Brien found that one in a hundred Caucasian Americans carries two copies of the defective gene—like Koup's patients, they are completely immune. One in five Caucasian Americans carries one copy of the mutant gene. Although these people can become infected, typically they stay healthy two to three years longer than those without any copies of the altered gene. O'Brien speculates that the reason may be that they have only half as many CCR5 receptors as is normal. "And half as many receptors probably limits the spread of virus and slows down the whole damn thing."

However, the defective gene shows up much more rarely in African Americans, and almost never in native Africans, or Asians. Why not? The answer must lie in the gene's origin. The resistance gene in O'Brien's genetically immune mice probably arose during an ancient viral outbreak and came down through the generations to the present day. He suspects

a similar origin for this human gene—but with one major difference. It must be relatively new, stemming from a time after the ancestors of the first Caucasians made their way out of Africa.

"We're thinking that the mutation probably took place on the order of 100,000 years ago," O'Brien says. "And because of the unusual nature of the mutation—that big deletion in the middle of the gene—we think it probably occurred in just one person. You hardly ever see dramatic mutations like this when you scroll through human genes—natural selection gets rid of

them. But not this time."

All of which leads to a knotty question. One hundred thousand years is a blink of an eye in evolutionary terms, hardly long enough for one lonely mutation, by chance, to gradually proliferate until it shows up in as much as 20 percent of a given population. "How in the hell did the gene get to be so frequent?" wonders O'Brien. "Something like that doesn't just happen by chance. Something jacked it up."

That something might have been a devastating epidemic that killed off much of the population while sparing those carrying the defective gene, which, presumably, protected them. Those survivors, who now made up a large percentage of the depleted population, passed the gene to their offspring. Given that kind of jump start, the gene might have spread to the millions who carry it today. "It could have been a prehistoric HIV that came in and wiped out large numbers of Caucasians," says O'Brien. "It could have been cholera, flu, bubonic plague. At least a quarter of the people in medieval Europe died from plague. That's a hell of a selective pressure."

But all that is conjecture. "We don't know anything about bubonic plague and chemokines. We don't know anything about flu and chemokines. We didn't even know what a chemokine receptor was until a few months ago. So when I give talks now I get these infectious-disease guys aside and ask them, 'Does your pathogen use this receptor?'"

Meanwhile, the frantic pace of research continues, now with an emphasis on translating these new findings into

practical treatments. Levy, who is not convinced that chemokines are the major mechanism in CAF, continues to try to pin down his elusive antiviral factor. (Over a decade later, his original patient remains healthy.) Gallo, for his part, is convinced. His team is attempting to demonstrate chemokines' essential role in protection by injecting them into monkeys and then exposing the animals to virus. If the chemokines succeed in preventing infection, the next step may be to design a vaccine that provokes the immune system to boost chemokine production in the presence of HIV.

Berger and Moore are independently trying to figure out how cell and virus interact, in the hopes of interfering with the process. Their hopes are high because seven-transmembrane receptors, the family to which CCR5 and fusin be-

long, are so familiar. "They have been major targets of drugs for other diseases," says Berger. "About a third of the top 40 best-selling drugs target seven-transmembrane receptors. I'm sitting here with an inhaler for my asthma, and that's targeting a seven-transmembrane receptor." As a result, scientists have a leg up in looking for compounds that block the receptors, so as to block HIV's access to cells. Landau and Littman are also among those in the hunt.

Littman is trying as well to produce a genetically engineered mouse that displays human CCR5 and fusin receptors on its cells. Such an animal would provide a living laboratory in which to investigate the process of infection and disease. "Getting a good animal model is the only way to understand

Freedom to Share

the mechanism of pathogenesis," he says. "Besides, even if we understand the molecular processes in the cell much better, eventually we have to confirm anything we do in an animal."

Others are looking into the possibility of providing the protective gene to infected people via gene therapy and bone marrow transplants. It might also be possible to devise a drug that disables the protein that forms the CCR5 receptor. These strategies appear promising because, in the case of CCR5 at least, those who carry defective versions of the gene for the receptor seem otherwise unaffected. In other words, the normal gene appears to play no discernible role in life—we can do without it just fine. "It's as if Mother Nature just handed this gene to us," says Landau. "It gives you optimism that you can knock it out without hurting anybody."

And there might be other mutations that block HIV. It's unlikely that Caucasians are the only ones to have evolved genetic resistance—people of African and Asian descent probably have their own defense mechanisms. Many populations include uninfected high-risk people, among them many Africans and Asians, and most don't carry the defective gene. Something else must be protecting them. Landau and Koup are among those looking for what that might be. "It could be a tiny mutation, something that's not obvious," Koup says. "This one was too easy. Usually it's not easy at all."

O'Brien is also searching for protective genes. "This isn't going to be the last gene that gets discovered," he says. "I think that by the end of the year we're going to be able to say that this gene contributes this percentage of protection, that gene contributes that percentage of protection—until we can account for much of the genetic component of infection." Nor does he think that AIDS is the only disease in which protective genes play a role. "We can go after other diseases, such as hepatitis, which is a leading cause of deaths from cancer, and prostate cancer and breast cancer. We're going to pin down some of these hidden genes."

But he might not agree that the process of discovery has been easy. He's been at it too long for that. "There were plenty of people who told me that looking for human resistance genes was likely to fail. They didn't think there was any evidence for such genes."

So much for that argument. ▢





Sale ends today

TRY A DIGITAL SUBSCRIPTION AND SAVE

NEWS

VIDEO

PEOPLE

VOICES

SPORT

TECH

LIFE

PROPERTY

A

UK ▾ / World ▾ / Business ▾ / People / Science / Environment ▾ / Media ▾ / Technology

News

The man who can't catch Aids

Discovery may lead to vaccine

TOM WILKIE SCIENCE EDITOR | Friday 29 March 1996



SHARE



TWEET



SHARE



REDDIT



SHARE



Scientists have found a man who cannot catch the virus that causes Aids - and his blood may hold the key to developing the first vaccine. In his blood, the New Yorker, Steve Crohn, has the first known substance in the world that will defeat the HIV virus. Scientists already knew of many individuals who remain healthy for a very long time between infection with HIV and developing full blown Aids. The difference in the case of Mr Crohn and the others now identified is that they appear to be resistant to infection with HIV in the first place. Mr Crohn, 49, a freelance editor for Fodor's Travel Guides, and another New Yorker who also appears to be immune, were discovered by a young Glaswegian scientist, Dr Bill Paxton, of the Aaron Diamond Aids Research Center in New York. Dr Paxton and his colleagues have found a further 23 people who, although not completely immune, show some degree of resistance to HIV infection. Many have remained free of HIV despite a history of unsafe sex with multiple sexual partners who subsequently died of Aids.

From these individuals, Dr Paxton and his colleagues have taken the white blood cells, known as CD4 cells, which are the particular target of HIV, cultured the cells in the laboratory, and tried unsuccessfully to infect them with HIV. In the case of Mr Crohn's cells, the researchers could only get the infection to "take" by flooding the cultured cells with huge amounts of virus, far more than would be present in the course of a naturally occurring form of infection. There have been indications that some people might be resistant to HIV infection, because of the chance shuffling of the genes they inherited from their parents. But this evidence is only statistical. The new research has identified specific individuals and their biochemistry to work out the precise mechanism of resistance. Dr Paxton said yesterday, "If we can determine what is protecting these people then you can envisage therapy or vaccine design." Dr Paxton and his colleagues have already identified one set of biochemical compounds, known as chemokines, which appear to be acting in these people to defeat HIV. These substances were first recognised only five years ago and appear to play a role in the immune system. They report their findings in the April issue of the scientific journal Nature Medicine. Conventional vaccines consist of antibodies to the infecting agent produced by the immune system. But, partly because HIV subverts the cells of the immune system itself and partly because it is highly variable, no one has succeeded in producing a vaccine against it. The chemokines Dr Paxton and his colleagues have found are not antibodies. They are involved in the "inflammatory" response, when a wound or site of infection becomes inflamed. "I do not believe that next week everybody will be injecting chemokines and curing Aids, but definitely we're on a line," Dr Paxton said. He stressed that any vaccine or treatment was still a long way off: "I'm really worried about how people will take this news - people should not give up a safe sex policy." For Mr Crohn, the thought that his blood might hold a vital secret in the battle against Aids "would be very touching to me." His partner, Jerry Greenwood, died in 1982, before the disease even had a name.

AIDS and the black death

A new PBS documentary connects HIV and the plague through people like Steve Crohn, whose ancestors' immunity to the black death has made them resistant to HIV **By Lawrence Ferber**

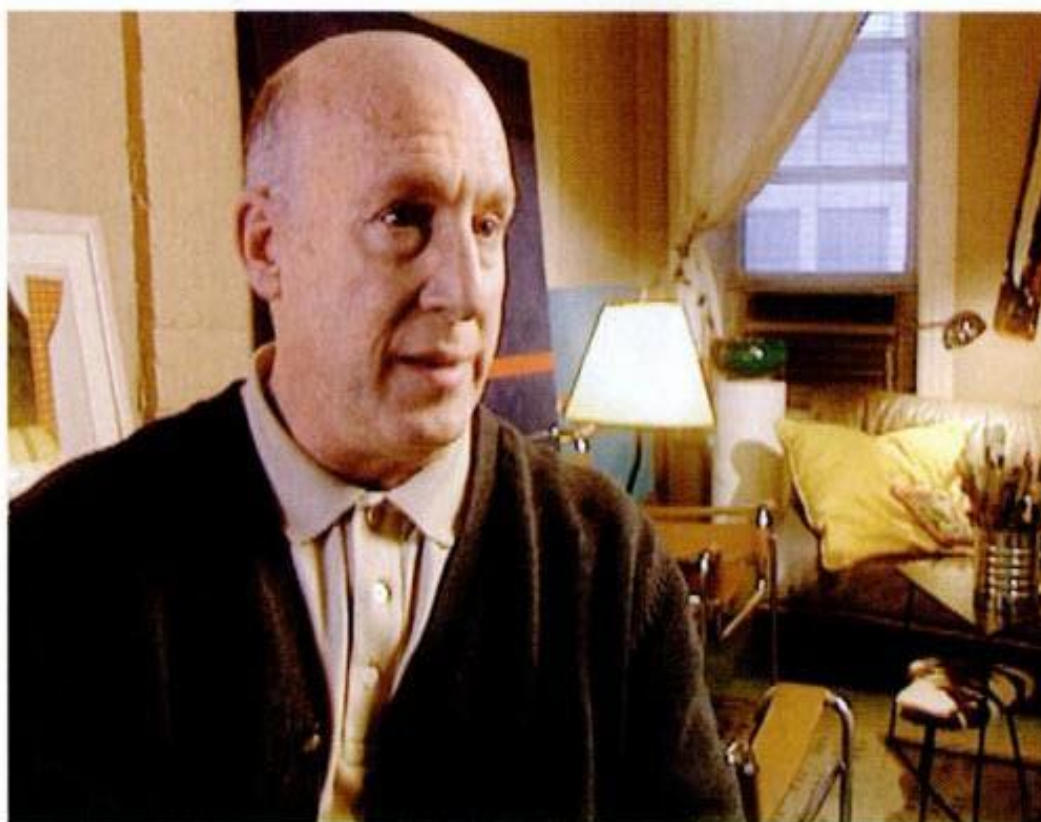
Few people can say with certainty that their ancestors had immunity to the black death that devastated Europe in the Middle Ages. New Yorker Steve Crohn can. What's more, the genes he inherited from those fortunate forebears may have made him largely immune to HIV.

Featured on "Mystery of the Black Death," the October 30 episode of PBS's *Secrets of the Dead* series, Crohn, 55, is a deep-voiced, no-bullshit freelance editor—and a survivor from the generation of gay New Yorkers swept away by the earliest wave of AIDS in the 1980s. Crohn's lover at the time, Jerry Green, was the fifth person in the United States reported to have died from AIDS complications. All but a handful of the couple's friends also succumbed to the scourge.

Crohn says he spent the 1980s waiting for his own demise. It never came. He repeatedly tested HIV-negative.

He eventually learned that he has a genetic mutation called Delta 32—a "defective" genotype that prevents his being infected by HIV-1, the most common strain of HIV. It's not a happenstance that Crohn takes lightly. "This has a spiritual meaning to me for a couple of reasons," he reflects. "I hate people saying 'I feel blessed'—I think that sounds so narcissistic."

Indeed, Crohn's participation in almost a decade of research into his genetic makeup—which may help others who do not have the Delta 32 mutation to battle HIV—has given him a profound sense of meaning. "It makes one feel like, yeah, you've been able to make a contribution," he says. "In some very small way your life has given



Steve Crohn in his New York apartment: His immunity to HIV-1, he says, "has a spiritual meaning."

something back. And this may affect the welfare and well-being of millions of people."

The *Secrets of the Dead* episode begins not with HIV but by investigating why so many residents of Eyam, England, survived the black death when it hit the remote village in 1665. Research by geneticist Stephen O'Brien has traced Crohn's Delta 32 mutation back hundreds of years to towns like Eyam, where the defensive genetic mutation held off the black death in much the same way it now protects Crohn from HIV. Today, about 10% of people of European heritage are estimated to be "Delta 32-heterozygous," which means they received the mutation from one parent and may have increased resistance to HIV. About 1% of that population, like Crohn, are Delta 32-homozygous, having inherited the genetic mutation from both parents.

Crohn learned about Delta 32 after he was enrolled in a 1994 Aaron Diamond AIDS Research Center study of

a dozen HIV-exposed individuals who remained seronegative over long periods of time. When Scottish researcher Bill Paxton mixed Crohn's CD4 immunity cells with HIV in the laboratory, "we could not establish an infection," Paxton recalls, "even with a high dose of HIV. This was something we had never seen before and was extremely provocative and exciting."

Researchers eventually learned that people with the Delta 32 mutation lack a functional gene coding for producing a receptor called CCR5—one of two chemical "locks" on the surface of CD4 cells that HIV can penetrate. The discovery has helped fuel research into drugs that would similarly block infection—although Paxton points out that HIV's ability to mutate may render many such drugs ineffective over time.

Crohn himself has long relied not on his theoretical immunity to avoid infection but on safer sex. "[Even if] there's another strain out there," he says, "I know I'm not being that exposed." ■

Stephen Crohn, 'The Man Who Can't Catch AIDS,' commits suicide at age of 66

As many of his friends died of AIDS, Stephen Crohn never became ill due to a genetic defect in his white blood cells. His sister confirmed that he took his own life last month.

BY JULIAN ARENZON, TRACY MILLER / NEW YORK DAILY NEWS / Published: Sunday, September 15, 2013, 11:18 PM
/ Updated: Monday, September 16, 2013, 6:43 PM

A A A



SHAYLASHAW VIA YOUTUBE

Steve Crohn, 'The Man Who Can't Catch AIDS,' is survived by his three sisters and several nieces and nephews.

RELATED STORIES

Vaccine cured monkeys of AIDS-causing virus: scientists

Sean Sasser, 'Real World' star and AIDS activist, dies at 44

Stephen Crohn, "The Man Who Can't Catch AIDS," took his own life late last month in New York at the age of 66.

Crohn's white blood cells had a genetic defect that made him resistant to AIDS even when tested with "HIV concentrations thousands of times greater than would be encountered outside a test tube," according to Dr. Bill Paxton of the Aaron Diamond AIDS Research Center in New York.

Crohn, a gay man, lost many friends and his partner, Jerry Green, to the disease at the height of the AIDS crisis in the 1980s - but never got sick himself.

"What's hard is living with the continuous grief," Crohn said in a 1999 interview for the PBS "Nova" documentary "Surviving AIDS."

"You kept losing people every year—six people, seven people. Last week, a friend of mine's obit. was in the paper. It's not easy, when you're losing friends and you're that young, and it goes on for such a long period of time. And the only thing you could compare it to would be to be in a war."

"My brother saw all of his friends dying, and he didn't die," Amy Crohn, Stephen's sister, explained to the [New York Times](#). "He went through a tremendous amount of survivor guilt about that and said to himself, 'There's got to be a reason.'"

Crohn volunteered himself for study at the Diamond center, where Paxton and Dr. David Ho discovered his genetic quirk: a flawed receptor, CCR5, that prevented HIV from infecting his CD4 white blood cells.



ANNIE-CHRISTINE POLIOLATI/AP/GETTY IMAGES

Scientists found that Crohn's white blood cells resisted infection when exposed to HIV, due to a rare genetic defect.

Paxton told The Times.

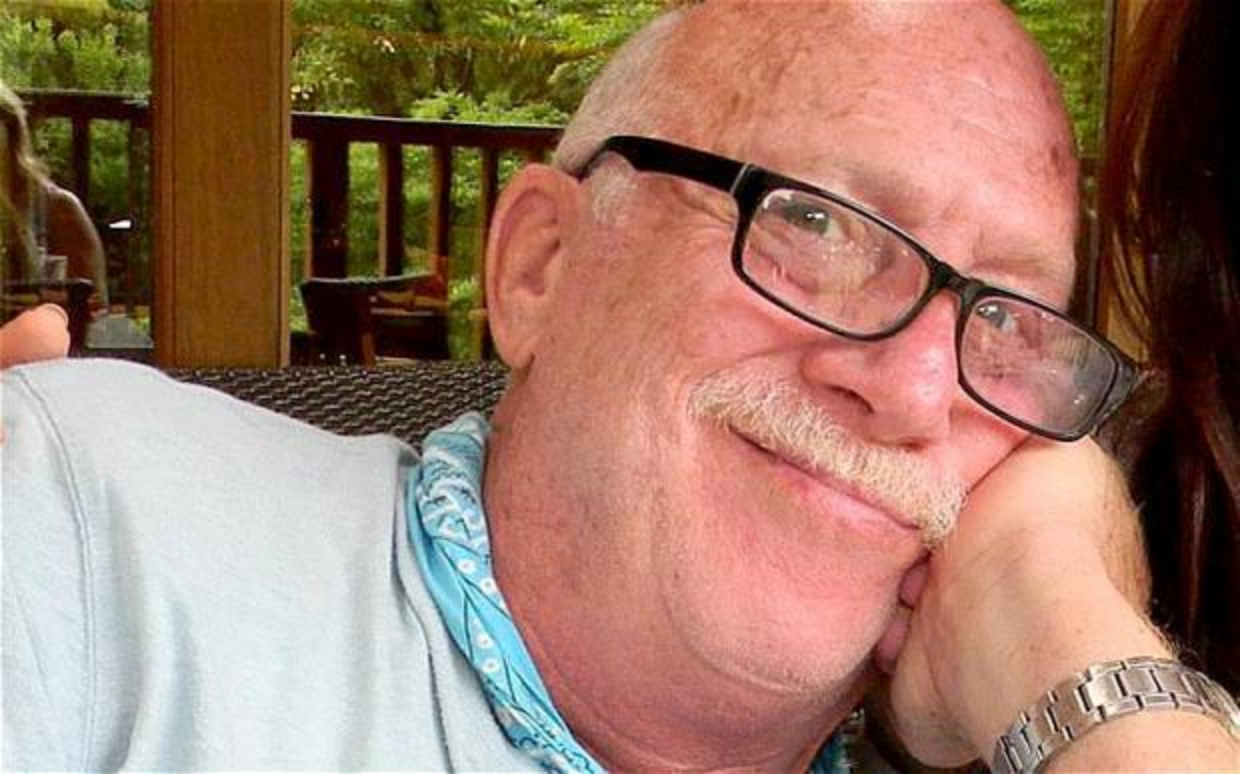
The groundbreaking discovery led to a greater understanding of how the HIV virus spreads in the body, as well as new treatments that continue to be used today. It also underlies ongoing research to find an effective AIDS vaccine.

In 1996, British newspaper [The Independent](#) called Crohn "The Man Who Can't Catch AIDS" - a title that came to define his life as he subsequently was the focus of documentary films and newspaper articles around the world.

Crohn, a painter and freelance editor for Fodor's Travel Guides, was raised in Dumont, N.J. and resided in New York City as an adult. He lived in Saugerties at the time of his death.

His great-uncle, Burrill B. Crohn, was a gastroenterologist who lent his name to Crohn's disease. Crohn felt he was carrying on his family's tradition by assisting in AIDS research.





Jeff Getty, 49; 1st Person to Receive Transplant of Marrow From Baboon

October 17, 2006 | Mary Rourke | Times Staff Writer

Jeff Getty, an AIDS patient and activist who in 1995 received the first baboon-to-human bone marrow transplant in an effort to prolong his life, died Oct. 9. He was 49.

Getty died of cardiac arrest at HiDesert Medical Center in Joshua Tree, Calif., his longtime partner Kenneth Klueh said Monday. He had been a resident of Joshua Tree for the last four years.

Getty was 38 when he elected to have the bone marrow of a baboon infused into his body. Surgery was performed Dec. 14, 1995, at San Francisco General Hospital. At the time he had been infected with HIV for 14 years and was told by doctors that he had less than one year to live.

Critics in the medical research community warned that the transplant could hasten Getty's death, in part because he could have animal viruses transmitted to him as a result of the procedure. Animal rights activists were opposed because the transplant required killing the baboon donor.

The highly experimental operation required the permission of the Food and Drug Administration, which Getty fought for two years to obtain.

"I'm going to die anyway," he told The Times in July 1995, once he had the FDA's approval. "Let's get on with finding some answers about the disease. If this saves me, then I got lucky."

Unlike humans, most primates are resistant to the HIV virus, Getty's doctors said before the surgery. The hope was that the baboon cells would take root in Getty's bones and fight off AIDS in his body.

Getty's body rejected the baboon cells. A number of scientists continued to follow his progress, concerned

Unlike humans, most primates are resistant to the HIV virus, Getty's doctors said before the surgery. The hope was that the baboon cells would take root in Getty's bones and fight off AIDS in his body.

Getty's body rejected the baboon cells. A number of scientists continued to follow his progress, concerned about the risk of new viruses from the baboon. Four years after the surgery, the FDA banned further such transplants.

During the first year after the procedure, Getty's health improved considerably. The reasons remained unclear. His doctors theorized that it could have been due, in part, to other treatments that he received in conjunction with the surgery, including radiation and chemotherapy.

"I have definitely bought some time," Getty told the New York Times in 1996.

He wanted to see transplant surgeries like his continue to be performed, with close monitoring.

"There's validity to being concerned about cross-species disease, but it shouldn't stop the research," he told the New York Times in 1998.

By the time of his controversial surgery, Getty was a well-known AIDS activist.

"Jeff was the consummate patient advocate," said Jeff Sheehy, a member of the governing board of the California Institute for Regenerative Medicine, an independent state agency.

Getty was a leader in the push to allow organ transplants for AIDS patients. In many cases, strong drug treatments damaged their livers or kidneys.

"The thinking was, 'Don't waste the healthy organ on someone whose prognosis is bleak,'" Sheehy told The Times on Monday.

Frustrated by that thinking, Getty threw a coffin on the lawn of a San Francisco hospital during a demonstration in 1999.

Now more surgeons are willing to perform organ transplants on HIV-positive patients.

As an activist, Getty also fought for "compassionate access" to AIDS drugs before they were approved by the FDA.

"Jeff argued with drug companies that people in desperate straits would survive longer if they could get access," Sheehy said

It is now common for experimental drugs to be made available to HIV patients, Sheehy said.

Born on July 14, 1957, in Connecticut, Getty moved to San Francisco in the 1970s, said Klueh, his partner of 26 years. They lived in Oakland through the 1990s before relocating to Joshua Tree.

Getty graduated from the New College of California in San Francisco, Klueh said. He was a journalism major.

He worked as an administrative analyst at UC Berkeley from 1980 until 1988.

Through the 1990s, he was increasingly visible as a leader of the advocacy group ACT UP Golden Gate.

In addition to Klueh, Getty is survived by his father, Edward; and three sisters. A memorial service is pending.

Contributions in his name can be made to Maitri Compassionate Care, 401 Duboce Ave., San Francisco, CA 94117, or on the website www.maitrisf.org.

*



BLOOD
DRIVE

BLOOD
DRIVE

ONE LIFE - GIVE BLOOD



Home » [Hutch News](#) » Doctor who cured 'Berlin patient' of HIV: 'We knew we were doing something very special'

HUTCH NEWS

Share

Doctor who cured 'Berlin patient' of HIV: 'We knew we were doing something very special'

Dr. Gero Hütter and Timothy Ray Brown speak about the transplant that forever linked them in medical history

Feb. 27, 2015 | By Mary Engel / Fred Hutch News Service



Dr. Gero Hütter, left, with Timothy Ray Brown. After Brown's cure became public, Hütter said he received emails daily from people with HIV saying "Please doctor, do the same for me."
Photo by Robert Hood / Fred Hutch News Service

When Dr. Gero Hütter gave **Timothy Ray Brown** a bone marrow transplant at a Berlin hospital on Feb. 7, 2007, he knew he could be making history. If, that is. Brown survived long enough to see whether the grueling transplant cured not only his leukemia but also his infection with HIV, the virus that causes AIDS.

Brown did survive, and eight years later, is free of both cancer and HIV. On Thursday, the German doctor reunited with his Seattle-born patient for a rare joint public appearance to talk about how the world's first -- and so far only -- HIV cure came about and what it means for the future.

"At the time we were doing the transplant, we knew we were doing something very special that could change the whole medical world if it worked," Hütter told a standing-room-only crowd of more than 200 people -- including Brown's mother -- at the downtown Seattle Public Library. "We weren't clear what would happen. It was a big and good surprise that it worked."

Added Brown: "I didn't really believe I was cured until he published the paper [in the *New England Journal of Medicine* in 2009]."

Identified only as "the Berlin patient" in that first paper and in subsequent media reports, Brown, 48, went public in 2010, around the time he returned from Berlin to live in the United States.

"I decided I needed to tell my story so other people could get cured as well," he said. "I decided I was going to be an activist for a cure for HIV."

At Thursday's talk and during a visit earlier in the day to Fred Hutchinson Cancer Research Center -- which **pioneered bone marrow transplants** and is now home to a **research consortium on curing HIV** -- Hütter talked about what it was like to be the doctor who brought about the cure.

The idea

An oncologist by training, Hütter, 45, is the first to admit that he didn't know much about HIV. But like many doctors who came of age or trained in the 1980s or early 1990s -- before antiretroviral therapy revolutionized AIDS treatment, for those who have access to and can tolerate the drugs -- he was deeply affected by the epidemic.

"I was very scared of HIV when it came out in the '80s," he said. "It was my time when my sexual activity started. I was scared of this thing. When I started medical school in 1992, there was no active treatment, and I saw people die."

That was why a paper he read while in medical school made such an impression on him. It described a rare genetic mutation called the CCR5 delta-32 deletion, which confers natural resistance to HIV. The mutation prevents CD4 cells -- infection-fighting white blood cells that HIV targets -- from developing a receptor, called a CCR5, on their surfaces. HIV uses this receptor to enter the cell. Without it, it's as though HIV is left standing at the door without a key to get in.

HIV targets -- from developing a receptor, called a CCR5, on their surfaces. HIV uses this receptor to enter the cell. Without it, it's as though HIV is left standing at the door without a key to get in.

"I was so impressed as a student that I kept this information for 10 years in my mind," Hütter said. "When Timothy came and I saw he had leukemia and HIV, it was clear to me that we had to find a donor who had this mutation."

said. "When Timothy came and I saw he had leukemia and HIV, it was clear to me that we had to find a donor who had this mutation."

Guinea pig

For his part, Brown wasn't interested in "being a guinea pig," he said. He was far more concerned about his new diagnosis -- **acute myeloid leukemia** -- than his old one. He had learned in 1995 that he was infected with HIV, but a year later, antiretroviral therapy was found to control it. So he hoped to be able to cure his cancer with chemotherapy rather than a riskier transplant. But when chemotherapy failed, he agreed to Hütter's plan to try to cure both.

The transplant itself was no different from what any patient with leukemia would undergo except that it required an additional step beyond the already complex process of finding a tissue-type match between donor and patient: A matching donor also had to have two copies of the CCR5 mutation, one from each parent.

It helped that Germany, where Brown was living at the time, had a large, centralized registry of stem cell donors, and the CCR5 mutation is most common in northern Europeans. Testing for the mutation is fairly simple and cost only an additional \$500, Hütter said. Brown had a high number of tissue-type matches -- 232. The 61st one tested had both copies of the mutation.

Hütter turned to data from Fred Hutch, amassed from years of transplant research, to assure himself that stem cells with the mutation would not adversely affect the leukemia treatment. (On Thursday -- his first actual visit to the Seattle campus -- he said, "For a hematologist, the Hutch is the Holy Grail.")

As is typical for a stem cell transplant, Brown underwent "conditioning," an intense chemotherapy and radiation regimen that destroys the immune system to make room for transplanted immune cells to grow. On the day of the transplant -- in a ward of the Berlin hospital named after a patient treated at Fred Hutch -- he stopped taking his antiretroviral medication.

"The key reason I believed it would work is because [Hütter] was so certain it would work," Brown said.

'At the right place at the right time'

Hütter did not sugar-coat the rigors of the transplant itself. Nor did he outright promise an HIV cure, as hopeful as his plan seemed.

"It made sense that it would work," he said. But there were risks, beyond the transplant itself. For one thing, sensitive tests done before the transplant had found that in addition to the strain of HIV that uses the CCR5 receptor to enter cells, Brown harbored traces of a rarer strain that uses a different receptor. Even if the transplant prevented infection by the more common strain, it was possible that the other strain would emerge to re-infect him.

"That would be a bad situation," Hütter said. "But you can treat it [with antiretrovirals]."

In addition, medicine, Hütter pointed out, "Is not always 100 percent. There will be patients for whom these procedures don't work."

In fact, in the years since Brown's treatment, efforts to replicate his cure have failed to show the same results, mostly because the patients died from the cancer or the transplant before it could be determined whether their HIV was gone. In one case, the rarer strain emerged. That has not happened with Brown.

Although ever the scientist, Hütter acknowledges the role that chance -- or luck if you have it -- played in Brown's cure. "He was at the right place at the right time," Hütter said, "undergoing treatment with an oncologist who remembered the 10-year-old HIV paper in a city with a good stem cell registry and access to a population with the needed mutation."

But he also points out the role that Brown played in his own treatment.

"What I admire about Timothy is his motivation," he said. "You can't cure cancer just with motivation. But when he came to us, he organized his life. The food was bad in the hospital, so he brought in his own food. He did workouts. Some patients lie in the bed and say, 'Doctor, come cure me.' He understood that he had to do his part. That's unusual. We had a good doctor-patient relationship."

The motivation was needed especially when Brown's leukemia -- though not his HIV -- returned a year later, and he needed a second transplant. Recovery from that one was much more difficult, leaving him needing to learn to walk and talk all over again.

While Hütter and Brown are very different on the outside -- one a married, mild-mannered scientist-physician, the other a gay activist who once modeled himself after Boy George -- they share a straightforward manner of speaking, a dry sense of humor and a professed lack of emotionalism that can belie their continued close relationship.

"We don't exchange Christmas cards," cracked Brown.

"I miss always his birthday," said Hütter.

The two men also share a passion in doing what they can to push for a cure for HIV that is easier, less risky and less expensive than what Brown endured and which everyone agrees is appropriate only for someone who needs a transplant primarily to cure cancer.

'Please doctor, do the same for me'

As an oncologist, Hütter was so unknown in the HIV field and a **cure was considered so unlikely** that it took almost a year after he first reported the results of Brown's transplant for a medical journal to publish his paper.

What Hütter revealed Thursday night was the immediate -- and overwhelming -- reaction to the case by people with HIV.

"After the case became public, I received nearly every day emails, requests from people with HIV, 'Please doctor, do the same for me, I give you any money,'" Hütter said. "I tried to answer every one. Sometimes it was my main work in a day to answer these questions."

Today, others are working hard on finding answers for patients desperate for a cure. Some, including the Hutch-based **defeatHIV consortium**, are using Brown's case as a blueprint for cure work centering on gene modification.

Led by virologist Dr. **Kaith Jerome** and stem cell and gene therapy specialist Dr. **Hans-Peter Kiem**, the plan is to take an HIV-infected person's own stem cells and knock out or disable the gene that acts as the HIV doorway, mimicking the genetics of someone who has natural resistance. The modified cells would then be returned to the patient.

Two other federally funded consortiums are investigating different approaches, and Hütter believes a cure will likely involve a mix, including a way to wipe out a reservoir of HIV that lies dormant in the body, hiding from antiretroviral therapy but roaring back if therapy is discontinued.

The overwhelming need for a cure was evident from the number of people who lined up Thursday evening to ask questions of Hütter and Brown. Perhaps the most poignant came from Moses Nsubaga, a member of the International Network for Strategic Initiatives in Global HIV Trials, who was visiting Seattle from Uganda.

"You are a symbol of hope in this struggle," he said to Hütter and Brown. "I come from a continent where you have 70 percent of the people living with HIV. People are hopeless. These days, they hear so much about Timothy Brown. When I go back to Africa, one of them will ask me, 'Is there a possibility of bringing Timothy to Africa so that he can interact with millions of people living with HIV?'"

"I definitely want to do that," Brown said. "I want to help."

Mary Engel is a staff writer at Fred Hutchinson Cancer Research Center. Previously, she was a writer covering medicine and health policy for newspapers including the Los Angeles Times, where she was part of a team that won a Pulitzer for health care reporting. She also was a fellow at the year-long MIT Knight Science Journalism program. Reach her at mengel@fredhutch.org.

Are you interested in reprinting or republishing this story? Be our guest! We want to help connect people with the information they need. We just ask that you link back to the original article, preserve the author's byline and refrain from making edits that alter the original context. Questions? Email editor Linda Dahlstrom at ldahlstr@fredhutch.org.

Subscribe to RSS

Editor's Picks

Immunotherapy offers 'new era' for cancer patients

Q&A: Alcohol and cancer risk: Distilling fact from fiction

Combating 'chemo mouth': Experts offer tips on countering metallic taste

GIVE NOW & SAVE LIVES

Support our quest for cures

\$ 100

DONATE NOW

For the Media

[News releases >](#)

[Media coverage >](#)

[Contact us >](#)

Story Archive

2015

[Jan](#)
[Feb](#)
[March](#)
[April](#)
[May](#)
[Nov](#)
[Dec](#)

2014

[Jan](#)
[Feb](#)
[March](#)
[April](#)
[May](#)

Publications

Quest

Our quarterly magazine

Annual Report

Fiscal year highlights

Science Spotlights

Monthly review of Center-authored papers

Fred Hutch News

Get updates via email.



Ray Brown
Foundation



Ray Brown
Foundation



Lifestyle | Thu Jan 2, 2014 5:21am EST

Relapse of 'cured' HIV patients spurs A

LONDON | BY KATE KELLAND, HEALTH AND SCIENCE CORRESPONDENT



Scientists seeking a cure for AIDS say they have been inspired, not crushed, by a major setback in which two HIV positive patients believed to have been cured found the virus re-invading their bodies once more.

True, the news hit hard last month that the so-called "Boston patients" - two men who received bone marrow transplants that appeared to rid them completely of the AIDS-causing virus - had relapsed and gone back onto antiretroviral treatment.

But experts say the disappointment could lay the basis for important leaps forward in the search for a cure.

"It's a setback for the patients, of course, but an advance for the field because the field has now gained a lot more knowledge," said Steven Deeks, a professor and HIV expert at the University of California, San Francisco.

He and other experts say the primary practical message is that current tests designed to detect even very low levels of HIV present in the body are simply not sensitive enough.

As well as having the human immunodeficiency virus (HIV), the Boston patients both also had a type of blood cancer called lymphoma, for which they were treated using bone marrow transplants - one man in 2008 and the other in 2010.

They continued taking the antiretroviral AIDS drugs, but eight months after each patient's transplant, doctors found they could not detect any sign of HIV in their blood.

In the early part of 2013, both patients decided to stop taking their AIDS drugs and both appeared to remain HIV-free - prompting their doctors, Timothy Henrich and Daniel Kuritzkes from Boston's Brigham and Women's Hospital, to announce at a conference in July that they may have been cured.

Yet in December came news that one of the men had begun to show signs of an HIV rebound by August, while the second patient had a relapse in November.

Henrich said the virus' comeback underlined how ingenious HIV can be in finding hiding places in the body to evade attack efforts by the immune system and by drug treatment.

"Through this research we have discovered the HIV reservoir is deeper and more persistent than previously known and that our current standards of probing for HIV may not be sufficient," he said, adding that both patients were "currently in good health" and back on antiretroviral therapy.

INSPIRATION

Barely a decade ago, few HIV scientists would have dared put the words HIV and cure in the same sentence. Yet some intriguing and inspiring cases in recent years mean many now believe it is just a question of time before a cure is found.

First was the now famous case of Timothy Ray Brown, the so-called "Berlin patient," whose HIV was eradicated by a complex treatment for leukemia in 2007 involving the destruction of his immune system and a stem cell transplant from a donor with a rare genetic mutation that resists HIV infection.

Such an elaborate, expensive and life-threatening procedure could never be used as a broad-spectrum approach for the world's 34 million HIV patients. But the results in Brown focused scientific attention on a genetic mutation known as 'CCR5 delta 32' as a target for possible gene therapy treatment.

Then last March, French scientists who followed 14 HIV-positive people known as the "Visconti patients", who were treated very swiftly with HIV drugs but then stopped treatment, said that even after seven years off therapy, they were still showing no signs of the virus rebounding.

That announcement came only weeks after news of the "functional cure" of an HIV-positive baby in Mississippi who received antiretroviral treatment for 18 months from the day she was born. By the time she was two this appeared to have stopped the virus replicating and spreading.

A "functional cure" is when HIV is reduced to such low levels that it is kept at bay even without treatment, though the virus can still be detected in the body.

Sharon Lewin, an HIV expert at Monash University in [Australia](#), said all these developments, as well as the setback suffered by the Boston patients, inspired scientists to investigate many different approaches in the search for a cure.

"We've learnt many things here - and one of the most important is that a tiny, tiny amount of virus can get the whole thing going again," she told Reuters. "It's a clear message that we need better ways to pick up the virus."

Scientists are now more convinced than ever that a two-pronged approach which aims to firmly suppress the virus while bolstering the immune system provides the best way forward.

"We need to attack in two ways - reduce the virus to very low levels and also to boost the immune response. We can't do one without the other," said Lewin.

"So we still have to think of other creative ways to control HIV. And it's still early days... before we can say which approach is likely to be the winner."

(Reporting by Kate Kelland, editing by Gareth Jones)

Genetic Engineering Can Cure Human Diseases

Animal Experimentation, 2002



Listen



Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

Listen

asana:

Move work forward.

Sign Up Free

Health

'Designer babies' debate should start, scientists say

By James Gallagher
Health editor, BBC News website

© 19 January 2015 | Health



Rapid progress in genetics is making "designer babies" more likely and society needs to be prepared, leading scientists have told the BBC.

Dr Tony Perry, a pioneer in cloning, has announced precise DNA editing at the moment of conception in mice.

He said huge advances in the past two years meant "designer babies" were no longer HG Wells territory.

Other leading scientists and bioethicists argue it is time for a serious public debate on the issue.

Designer babies - genetically modified for beauty, intelligence or to be free of disease - have long been a topic of science fiction.

Dr Perry, who was part of the teams to clone the first mice and pigs, said the prospect was still fiction, but science was rapidly catching up to make elements of it possible.

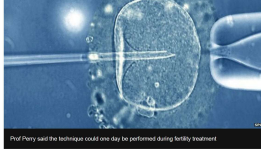
In the journal **Scientific Reports**, he details precisely editing the genome of mice at the point DNA from the sperm and egg come together.

Dr Perry, who is based at the University of Bath, told the BBC: "We used a pair of molecular scissors and a molecular sat-nav that tells the scissors where to cut.

"It is approaching 100% efficiency already, it's a case of 'you shoot you score'."

New era

It is the latest development of "Crispr technology" - which is a more precise way of editing DNA than anything that has come before.



Prof Perry said the technique could one day be performed during fertility treatment

It was named **one of the top breakthroughs in 2013**, hailed as the start of a new era of genetics and is being used in a wide-range of experiments in thousands of laboratories.

As well simply cutting the DNA to make mutations, as the Bath team have done, it is also possible to use the technology to insert new pieces of genetic code at the site of the cut.

It has reopened questions about genetically modifying people.

Prof Perry added: "On the human side, one has to be very cautious.

"There are heritable diseases coded by mutations in DNA and some people could say, 'I don't want my children to have these mutations.'"

This includes conditions such as cystic fibrosis and genes that increase the risk of cancer.

"There's much speculation here, but it's not completely fanciful, this is not HG Wells, you can imagine people doing this soon [in animals].

Wells, you can imagine people doing this soon [in animals].

"At that time the HFEA [the UK's fertility regulator] will need to be prepared because they're going to have to deal with this issue."

because they're going to have to deal with this issue."

He said science existed as part of a wider community and that it was up to society as a whole to begin assessing the implications and decide what is acceptable.

Time for debate

Time for debate

Prof Robin Lovell-Badge, from the UK Medical Research Council, has been influential in the debate around **making babies from three people** and uses the Crispr technology in his own lab.

He said testing embryos for disease during IVF would be the best way of preventing diseases being passed down through the generations.

However, he could see such potential uses of "germ-line therapies" for men left infertile by damaging mutations.

While they can have children through IVF, any sons would still have the mutations and would in turn need IVF. Genetic modification could fix that.

It would also be useful in circumstances when all embryos would carry the undesirable, risky genes.

undesirable, risky genes.

Prof Lovell-Badge told the BBC News website: "Obviously in the UK, this is not allowed and there would have to be a change in regulations, which I suspect would have enormous problems.

"But it is something that needs to start to be debated.

"There has been a blanket ban on germ-line therapy, so there needs to be a debate about that and some rational thought rather than knee-jerk reactions that, 'No you can't possibly do that.'"



Such a debate would also have to move beyond therapies into the field of babies designed to have desirable traits.

Some alterations would only require small changes to DNA, such as some changes to eye colour or to make a child HIV-resistant.

The respected Nuffield Council on Bioethics is understood to be considering a report on the issue.

a report on the issue.

Its verdict in 2012 that **it was ethical to create babies from three people** formed a core part of the public debate on the issue.

At the time it said a much wider debate on germ-line therapy was still needed.

Complex ethics

Complex ethics

Its director, Hugh Whittall, told the BBC: "I think this is a challenge, for all of us, we should get onto looking at this fairly rapidly now."

He said the field raised questions of social justice around techniques available only to the rich and what constituted identity as well as "issues of governance and regulation".

Dr David King, from the campaign group Human Genetics Alert, echoed calls for the public to engage with the issue.

for the public to engage with the issue.

He said: "I think it's pretty inevitable that we'll get to a point where it's scientifically possible, certainly these new techniques of genome editing have made something look much more feasible than it did five years ago.

"But that does not mean to say it's inevitably the way we have to go as a society."

This is still a matter of science fiction and there is a huge amount of research - particularly on unwanted mutations, efficiency and safety - that needs to be done before any attempt of humans would even be considered.

A spokesman for the UK's Human Fertilisation and Embryology Authority said: "We keep a watchful eye on scientific developments of this kind and welcome discussions about future possible developments."

He said it "should be remembered that germ-line modification of nuclear DNA remains illegal in the UK" and that new legislation would be needed from Parliament "with all the open and public debate that would entail" for there to be any change in the law.